



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
-----------------	-------------	----------------------	---------------------

09/469,812 12/22/99 STUIVER

M MOG57688/UST

EXAMINER

HM12/0328

LIZA D HOHENSCHUTZ
ZENECA AG PRODUCTS
P O BOX 15458
1800 CONCORD PIKE
WILMINGTON DE 19850-5458

KRUSE, D
ART UNIT PAPER NUMBER

1638
DATE MAILED:

03/28/01

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File Copy

Office Action Summary	Application No.	Applicant(s)
	09/469,812	STUIVER ET AL.
	Examiner David H Kruse	Art Unit 1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on _____.

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-11 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are objected to by the Examiner.

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:

- 1) Certified copies of the priority documents have been received.
- 2) Certified copies of the priority documents have been received in Application No. _____.
- 3) Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) Notice of References Cited (PTO-892)

16) Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4

18) Interview Summary (PTO-413) Paper No(s) _____

19) Notice of Informal Patent Application (PTO-152)

20) Other: _____

DETAILED ACTION

Interference

1. The following allowable claim is suggested for the purpose of an interference:

Claim 1. A method for producing a transgenic plant containing a polynucleotide of interest, the method comprising:

- (a) introducing into a plurality of plant cells a T-DNA vector comprising:
 - (i) a T-DNA sequence comprising a right border, a left border and the polynucleotide of interest positioned between the right border and left border, and
 - (ii) a non-T-DNA sequence comprising a barnase polynucleotide sequence encoding a barnase enzyme, wherein said non-T-DNA sequence is located beyond the left T-DNA border;
- (b) selecting a plant cell which comprises the T-DNA sequence and does not comprise the barnase polynucleotide sequence; and
- (c) regenerating a transgenic plant from the selected plant cell.

The suggested claim must be copied exactly, although other claims may be proposed under 37 CFR § 1.605(a).

Applicant should make the suggested claim within ONE MONTH or THIRTY DAYS from the mailing date of this letter, whichever is longer. Failure to do so will be considered a disclaimer of the subject matter of this claim under the provisions of 37

CFR § 1.605(a). THE PROVISIONS OF 37 CFR § 1.136(a) DO NOT APPLY TO THIS TIME PERIOD.

2. Applicant need not respond to the remaining issues in this action if a suggested claim is copied for the purpose of an interference within the time limit specified above (37 CFR § 1.605(b)).

Specification

3. This application does not contain an abstract of the disclosure as required by 37 CFR § 1.72(b). An abstract on a separate sheet is required.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

5. The following guidelines illustrate the preferred layout and content for patent applications. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

The following order or arrangement is preferred in framing the specification and, except for the reference to "Microfiche Appendix" and the drawings, each of the lettered items should appear in upper case, without underlining or bold type, as section headings. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) Title of the Invention.
- (b) Cross-References to Related Applications.
- (c) Statement Regarding Federally Sponsored Research or Development.
- (d) Reference to a "Microfiche Appendix" (see 37 CFR 1.96).
- (e) Background of the Invention.
 - 1. Field of the Invention.
 - 2. Description of the Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (f) Brief Summary of the Invention.
- (g) Brief Description of the Several Views of the Drawing(s).

- (h) Detailed Description of the Invention.
- (i) Claim or Claims (commencing on a separate sheet).
- (j) Abstract of the Disclosure (commencing on a separate sheet).
- (k) Drawings.
- (l) Sequence Listing (see 37 CFR 1.821-1.825).

6. The disclosure is objected to because of the following informalities:

There are two Table 1's on pages 7 and 13. The tables must be renumbered and any reference to the tables must be corrected in the Specification.

At page 9 there are missing parenthesis at lines 25, 28, 29, 32, 34 and page 12 at line 5.

The references to Fig. and Table should be capitalized, see pages 11, lines 15 and 33; page 12, line 34; page 13, line 17; page 14, line 9.

Appropriate correction is required.

Claim Objections

7. Claim 6 is objected to under 37 CFR § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically Claim 5 is limited to a vir box sequence and Claim 6 encompasses other sequences that could be unrelated to the vir box sequence.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-11 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant claims a vector for plant transformation, a method for obtaining transgenic plants and a host containing said vector wherein the vector comprises a nucleic acid sequence which prevents the development of plant transformants having more vector sequence than the T-DNA sequence between the left and right border sequences.

Applicant teaches a vector, transgenic plant cell and method of making wherein said transgenic plant cell has a reduced frequency of incorporation of T-DNA sequences beyond the left border sequence (see Example 7, page 14).

Applicant does not teach a vector or method of making a transgenic plant wherein incorporation of T-DNA sequences beyond the left border sequence is totally eliminated.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

The nature of the invention is such that total prevention of incorporation of T-DNA sequences beyond the left border is not possible. The use of toxic proteins or enzymes would require that a sequence encoding an active protein be transcribed every time in order to prevent incorporation of unwanted sequences. In addition, sequences beyond the left border would have to inhibit read through in an absolute manner in order to practice the invention as claimed. The unpredictability of the art in incorporating heterologous DNA sequences into plants using the Ti-plasmid has demonstrated that absolute control of transformation events using the Ti-plasmid model is not possible.

10. Claims 1- 4 and 6-11 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a vector comprising a barnase encoding DNA sequence, a GC clamp sequence comprising SEQ ID NO: 5 and 6, or a DNA sequence to which Vir G binds, to the left of the T-DNA left border sequence, a method of using said vector and a plant cell comprising said vector, does not reasonably provide enablement for a vector comprising a DNA sequence to the left of the T-DNA left border sequence encoding any toxic compound, any GC rich DNA sequence, or a sequence to which any DNA-binding protein interacts, a method of using said vector or a plant cell comprising said vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant claims a vector for plant transformation, a method for obtaining transgenic plants and a host containing said vector wherein the vector comprises a nucleic acid sequence which prevents the development of plant transformants having

more vector sequence that the T-DNA sequence between the left and right border sequences.

Applicant teaches a vector comprising a DNA sequence outside of the left T-DNA border that encodes a barnase RNase, a GC-rich DNA sequence comprising SEQ ID NO: 5 and 6, and a DNA sequence to which Vir G binds, a transgenic plant cell comprising said vector and method of making said cell wherein said transgenic plant cell has a reduced frequency of incorporation of T-DNA sequences beyond the left border sequence (see Example 7, page 14).

Applicant does not teach a vector comprising a DNA sequence outside of the left T-DNA border that encodes a toxic compound (other than a barnase-RNase), other GC-rich DNA sequences or DNA sequences that bind DNA-binding proteins (other than that which binds VirG), a transgenic plant cell comprising said vector and method of making wherein said DNA sequence reduces the frequency of incorporation of T-DNA sequences beyond the left border sequence.

The teachings of Wands are discussed above.

The state of the art for transformation of plants using a Ti plasmid vector system is unpredictable and it has been observed that transcriptional read through at the left border sequence can be problematic (Ramanathan *et al*, Plant Molecular Biology 1995, 28:1149-1154, see abstract). Applicant has only taught a vector and a method comprising a DNA sequence encoding a barnase outside of the left T-DNA border that acts as a negative selection marker for incorporation of T-DNA sequences outside of the left and right borders into a plant cell. In addition, Applicant has only taught a vector

and method of using wherein the vector comprises a VirG binding sequence outside of the left T-DNA border. The effects of heterologous DNA sequences on transgenic plants requires empiric experimentation. Thus, it would require undue trial and error experimentation, transforming a plant cell with a vector comprising a myriad of DNA sequence that encodes a toxic compound (*i.e.* an enzyme or toxin) that acts as a negative selection marker when incorporated into a plant cell or all known sequences to which DNA-binding proteins bind in order to practice Applicant's invention as broadly claimed.

At Claims 9 and 10, the "host" encompasses organisms other than plants and bacteria (such as humans) for which the specification is not enabled. An appropriate limitation to the enabled "host(s)" is required.

11. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

12. Claims 1-11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-11 are indefinite because they lack an article of language. Claims 1, 8, 9 and 11 should begin with -- A --, and Claims 2-7 and 10 should begin with -- The --. Appropriate correction is required.

At Claim 1, it is unclear what relationship the "nucleic acid sequence" at line 3, has with the T-DNA borders of line 2.

At Claim 1, it is unclear what the metes and bounds of the term “prevents” is in relationship to “development of plant transformants”.

At Claim 1 line 4, the metes and bound of the term “having” is unclear (e.g. transient transformation or incorporation in to the plant’s genome). It is unclear if the phrase “more vector sequence than the T-DNA sequence” encompasses the T-DNA border sequences, the T-DNA sequence normally includes a gene encoding an opine.

At Claim 2, the phrase “T-DNA sequence” at line 3 lacks a proper antecedent basis. The term “preferably” at line 4 is indefinite. The phrase “such as” at line 6 is indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention (see MPEP § 2173.05(d)).

Claim 2 is rejected as indefinite for being in improper Markush format. The Office recommends the use of the phrase “selected from the group consisting of...” with the use of the conjunction “and” rather than “or” in listing the species. See MPEP 2173.05(h).

Claims 3-7 are indefinite because they contradict Claim 1, in that prevention of “readthrough” occurs prior to transference of the T-DNA into the plant cell and thus would not affect “development of plant transformants”. Claims 3-7 are improperly dependant upon Claim 1 and thus must be canceled or Claim 3 must be rewritten in independent form.

At Claim 6, the phrase “high GC-content” is relative and does not state the metes and bounds of the claimed invention.

Claims 6 and 7 are improperly dependent upon Claim 5 because they do not further limit the “vir box having the sequence of SEQ ID NO: 19”, and should be dependent upon Claim 3.

Claims 6, 7 and 10 are indefinite because the term “preferably” and the phrase “more preferable” does not state the metes and bounds of the invention.

At Claim 8 line 2, the term “outside” is unclear, does Applicant mean “flanking” or “adjacent to the T-DNA left border”?

At Claims 8, 9 and 11, the phrase “a vector” should read -- the vector -- because it refers to a previously recited vector.

Claim 10 is indefinite because it is improperly dependent upon Claim 5 because Claim 5 does not recite a “Host”. It appears Claim 10 should be dependent upon Claim 9. Clarification or correction is required. In addition, at line 2, the word “memeber” should read -- member --.

Claim 11 is incomplete and thus does not distinctly claim the subject matter because no method steps are given.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-3 and 6-11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Ramanathan *et al.* (Plant Molecular Biology 1995, 28:1149-1154) in view of Odell *et al* (U.S. Patent 5,658,772).

Applicant claims a vector for plant transformation, a method for obtaining transgenic plants and a host containing said vector wherein the vector comprises a nucleic acid sequence which prevents the development of plant transformants having more vector sequence than the T-DNA sequence between the left and right border sequences.

Ramanathan teaches a vector and a method of transforming plant cells comprising a Ti-plasmid system using the *Agrobacterium* method. Ramanathan teaches that T-DNA sequences beyond the left border sequence are transferred during plant transformation and that it would be desirable to incorporate a second selection marker adjacent to the left border to help identify transformants which have obtained both the T-DNA and non-T-DNA regions or incorporate a stop-transfer signal adjacent to the left border (see pages 1152-1153, the spanning paragraph).

Ramanathan does not teach incorporation of a toxin encoding sequence adjacent to the left T-DNA border, or a stop-transfer signal.

Odell teaches the coding region of barnase is highly effective in disrupting the function of plant cells (column 12, lines 57-60).

At Claims 1, 2 and 8-11 it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to use the barnase coding

region of Odell to modify the method of Ramanathan in order to incorporate a negative selection marker for cells transformed with DNA sequence outside of the T-DNA region. Because Odell was able to demonstrate tissue disruption by activating a barnase encoding gene in a transgenic plant cell, one of ordinary skill in the art would have had a reasonable expectation of success (see Example 13, columns 42-48).

At Claims 3, 6 and 7 it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the method of vector of Ramanathan to incorporate a GC rich sequence adjacent to the left border of the T-DNA region in order to increase the energy required to unwind the DNA in the GC rich region. It has been long recognized in the art that GC rich regions of DNA are thermodynamically highly stable and resist conformational changes. Such regions are known to resist transcription, often causing DNA polymerases to fall off such regions of DNA during replication. Given the known characteristics of GC rich regions of DNA, one of ordinary skill in the art would have had a reasonable expectation of success in inhibiting read-through if a GC region was incorporated into a vector adjacent to the T-DNA region.

15. Claims 4 and 5 are free of the prior art of record because use of the VirG DNA-binding region sequence to prevent read-through during DNA transcription was not taught or reasonably suggested by the prior art.

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Paula Hutzell can be reached at (703) 308-4310. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Yolanda Vines whose telephone number is (703) 305-2365.



**AMY J. NELSON, PH.D
PRIMARY EXAMINER**

David H. Kruse, Ph.D.
19 March, 2001